For previously untreated follicular, CD20-positive, B-cell NHL in combination with CVP chemotherapy

RITUXAN+CVP provides significant improvement in PFS in patients with follicular NHL

Up to 8 cycles of R-CVP significantly improved PFS over CVP* alone

RITUXAN+CVP as first-line treatment improves median PFS[1,2]

In first-line follicular NHL
At 4.4-year follow-up

2.83 years R-CVP vs **1.25 years** CVP

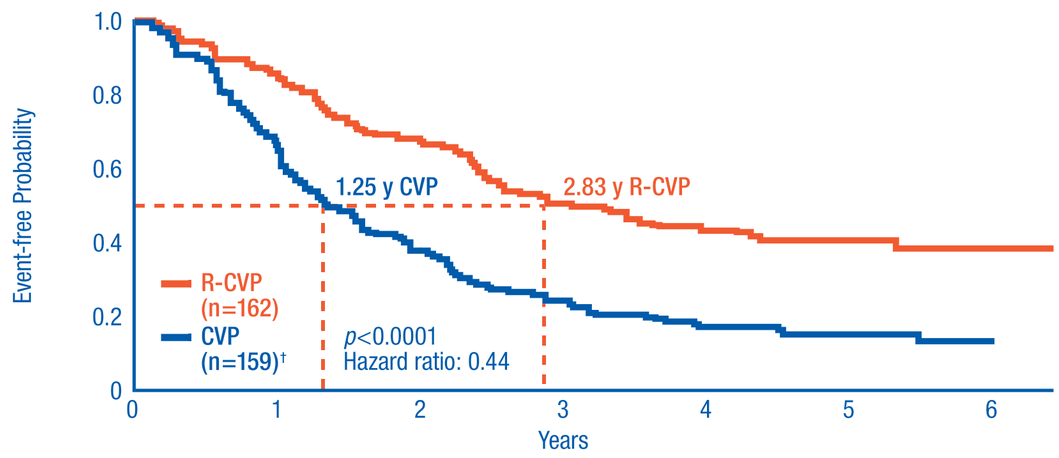
127% improvement in median **PFS**

Marcus (M39021) trial

Efficacy summary

- R-CVP more than doubled median PFS at 4.4 years of follow-up[1,2]
- Median PFS was improved by 71% (2.4 years vs 1.4 years) at 1.5-year follow-up[2]
- The R-CVP benefit was consistent across patient subgroups, including bulky disease and poor-prognosis FLIPI score[3]

Marcus progression-free survival (N=322)[1,4]



Marcus protocol: R-CVP ×8 vs CVP ×8[2,3]

- Patients (N=322) were randomized to receive 8 three-week cycles of R-CVP (n=162) or 8 three-week cycles of CVP (n=160)
- Primary endpoints: PFS, TTF

Marcus trial: Previously untreated, advanced-stage patients[4]

Baseline patient characteristics		R-CVP (n=162)	CVP (n=159)†
Age range (years)		27–79	29–80
Median age		52	53
Elevated LDH (>1×ULN)		26%	26%
Ann Arbor Stage	I/II	1%	1%
	III/IV	99%	99%
ECOG performance status	0–1	98%	95%
	2	3%	5%
Bulky disease (>7 cm)		39%	46%
Number of nodal sites	<5	18%	16%
	≥5	82%	84%
FLIPI index	0–2	53%	50%
	3–5	47%	50%

*CVP=cyclophosphamide, vincristine, and prednisolone.
†One patient assigned to the CVP group did not receive any trial medication because this patient withdrew consent.[4]
CD=cluster of differentiation; NHL=non-Hodgkin's lymphoma; R-CVP=RITUXAN plus CVP; R=RITUXAN 375 mg/m^2, given on the first day of each CVP cycle; PFS=progression-free survival; FLIPI=Follicular Lymphoma International Prognostic Index; LDH=lactate dehydrogenase; ECOG=Eastern Cooperative Oncology Group; TTF=time to treatment failure.

Most frequent adverse reactions in the study of RITUXAN in combination with CVP for previously untreated follicular NHL

Patients in the R-CVP arm had higher incidences of infusional toxicity and of neutropenia as compared with those in the CVP arm. The following adverse reactions occurred more frequently (≥5%) in patients receiving R-CVP compared with CVP alone: rash (17% vs 5%), cough (15% vs 6%), flushing (14% vs 3%), rigors (10% vs 2%), pruritus (10% vs 1%), neutropenia (8% vs 3%), and chest tightness (7% vs 1%).[2]

Attention Healthcare Provider: Provide Medication Guide to patient prior to RITUXAN infusion.

Important safety information is featured on a separate panel. For additional safety information, please see the full prescribing information, including **BOXED WARNINGS** and Medication Guide, available at this exhibit.

References: 1. Marcus R, Imrie K, Catalano J, et al. Rituximab plus CVP improves survival in previously untreated patients with advanced follicular non-Hodgkin's lymphoma. Paper presented at: American Society of Hematology 48th Annual Meeting and Exposition; December 9-12, 2006; Orlando, FL. Abstract 481. **2.** RITUXAN® (Rituximab) full prescribing information, Genentech, Inc., 2008. **3.** Marcus R, Imrie K, Belch A, et al. CVP chemotherapy plus rituximab compared with CVP as first-line treatment for advanced follicular lymphoma. *Blood*. 2005;105:1417-1423. **4.** Data on file, Genentech, Inc.

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For previously untreated diffuse large B-cell, CD20-positive NHL
in combination with CHOP or other anthracycline-based chemotherapy regimens

RITUXAN+CHOP is proven to increase overall survival in DLBCL

First combination to extend DLBCL survival since the 1970s

RITUXAN+CHOP as first-line treatment increases OS in DLBCL[1,2]

In first-line DLBCL
At 7 years

53% R-CHOP vs **36%** CHOP

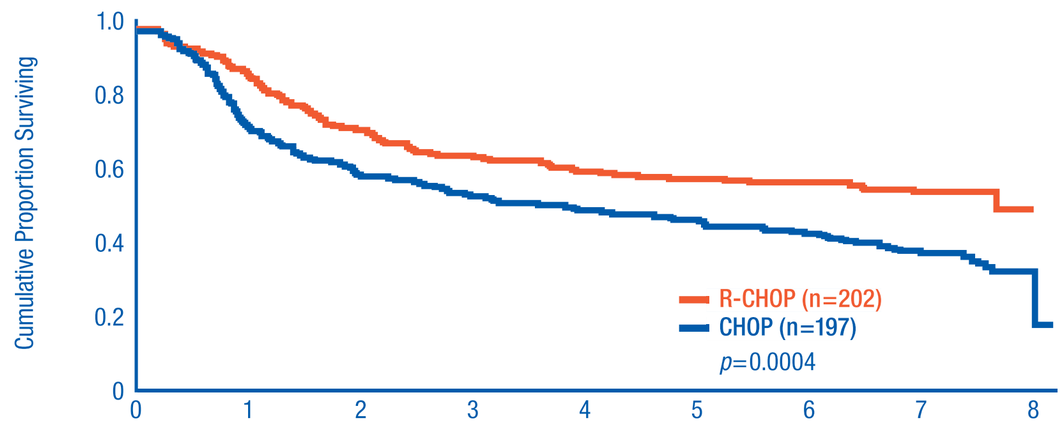
47% increase in OS

GELA LNH 98-5 trial

Efficacy summary

- R-CHOP improved 7-year OS by 47% vs CHOP* alone (p=0.0004)[1,2]
- 5-year OS was 58% for 8 cycles of R-CHOP vs 46% for CHOP alone[2]
- 164% improvement in the primary endpoint, EFS, at 2-year follow-up (2.9 years vs 1.1 years, p<0.001)[3]

GELA overall survival (N=399)[1,3]



GELA protocol: R-CHOP ×8 vs CHOP ×8

- Patients (N=399) were randomized to receive 8 three-week cycles of R-CHOP (n=202) or up to 8 three-week cycles of CHOP alone (n=197)[3]
- Primary endpoint: EFS[3]

GELA LNH 98-5 trial: Elderly DLBCL patients[3]

Baseline patient characteristics		R-CHOP (n=202)	CHOP (n=197)
Age range (years)		59–80	60–80
Median age		70	69
Elevated LDH (>1×ULN)		65%	67%
Ann Arbor Stage	I/II	20%	21%
	III/IV	79%	80%
ECOG performance status	0–1	78%	84%
	2–3	22%	17%
Bulky disease (>10 cm)		30%	33%
Extranodal involvement (≥2)		52%	52%
IPI score†	<2	40%	39%
	≥2	60%	61%

*CHOP=cyclophosphamide, doxorubicin, vincristine, and prednisone.
†In the GELA trial, the age-adjusted IPI score, which ranged from 0 to 3, was derived by assigning 1 point for each of the following risk factors: Ann Arbor Stage III or IV, ECOG performance status ≥2, and elevated LDH.
CD=cluster of differentiation; NHL=non-Hodgkin's lymphoma; DLBCL=diffuse large B-cell lymphoma; R-CHOP=RITUXAN plus CHOP; R=RITUXAN 375 mg/m^2, given on the first day of each CHOP cycle; OS=overall survival; EFS=event-free survival; GELA=Groupe d'Etude des Lymphomes de l'Adulte; LDH=lactate dehydrogenase; ECOG=Eastern Cooperative Oncology Group; IPI=International Prognostic Index.

Most frequent adverse reactions (all grades) in RITUXAN DLBCL studies

The following adverse reactions, regardless of severity, were reported more frequently (≥5%) in patients ≥60 years of age receiving R-CHOP as compared with CHOP alone: pyrexia (56% vs 46%), lung disorder (31% vs 24%), cardiac disorder (29% vs 21%), and chills (13% vs 4%). A review of cardiac toxicity determined that supraventricular arrhythmias or tachycardia accounted for most of the difference in cardiac disorders (4.5% for R-CHOP vs 1.0% CHOP).[2]

Grade 3–4 adverse reactions in RITUXAN DLBCL studies

The following Grade 3 or 4 adverse reactions occurred more frequently among patients in the R-CHOP arm compared with those in the CHOP arm: thrombocytopenia (9% vs 7%) and lung disorder (6% vs 3%). Other Grade 3 and 4 adverse reactions reported more frequently among patients receiving R-CHOP were viral infection, neutropenia, and anemia.[2]

Attention Healthcare Provider: Provide Medication Guide to patient prior to RITUXAN infusion.

Important safety information is featured on a separate panel. For additional safety information, please see the full prescribing information, including **BOXED WARNINGS** and Medication Guide, available at this exhibit.

For more information about GELA and other DLBCL trials (E4494 and MInT), please see the RITUXAN full prescribing information, including **BOXED WARNINGS** and Medication Guide, available at this exhibit.

References: 1. Coiffier B, Feugier P, Mounier N, et al. Long-term results of the GELA study comparing R-CHOP and CHOP chemotherapy in older patients with diffuse large B-cell lymphoma show good survival in poor-risk patients. *J Clin Oncol*. 2007;25(suppl 18S):443s. Abstract 8009. **2.** RITUXAN® (Rituximab) full prescribing information, Genentech, Inc., 2008. **3.** Coiffier B, Lepage E, Brière J, et al. CHOP chemotherapy plus rituximab compared with CHOP alone in elderly patients with diffuse large-B-cell lymphoma. *N Engl J Med*. 2002;346:235-242.

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BOXED WARNINGS and Additional Important Safety Information

WARNING: FATAL INFUSION REACTIONS, TUMOR LYSIS SYNDROME (TLS), SEVERE MUCOCUTANEOUS REACTIONS, and PROGRESSIVE MULTIFOCAL LEUKOENCEPHALOPATHY (PML)[1]

Infusion Reactions: RITUXAN administration can result in serious, including fatal infusion reactions. Deaths within 24 hours of RITUXAN infusion have occurred. Approximately 80% of fatal infusion reactions occurred in association with the first infusion. Carefully monitor patients during infusions. Discontinue RITUXAN infusion and provide medical treatment for Grade 3 or 4 infusion reactions.[1]

Tumor Lysis Syndrome (TLS): Acute renal failure requiring dialysis with instances of fatal outcome can occur in the setting of TLS following treatment of non-Hodgkin's lymphoma (NHL) patients with RITUXAN.[1]

Severe Mucocutaneous Reactions: Severe, including fatal, mucocutaneous reactions can occur in patients receiving RITUXAN.[1]

Progressive Multifocal Leukoencephalopathy (PML): JC virus infection resulting in PML and death can occur in patients receiving RITUXAN.[1]

RITUXAN has also been associated with fatal hepatitis B reactivation with fulminant hepatitis, other serious viral infections, cardiovascular events, renal toxicity, and bowel obstruction and perforation.[1]

The most common adverse reactions of RITUXAN (incidence ≥25%) observed in patients with NHL are infusion reactions, fever, chills, infection, asthenia, and lymphopenia. The incidence of infusion reactions was highest during the first infusion (77%) and decreased with each subsequent infusion. These infusion reactions generally have resolved with slowing or interruption of the infusion and with supportive care.[1]

RITUXAN in Combination with CVP for Previously Untreated, Follicular NHL

Patients in the R-CVP arm had higher incidences of infusional toxicity and of neutropenia as compared to those in the CVP arm. The following adverse reactions occurred more frequently (≥5%) in patients receiving R-CVP compared to CVP alone: rash (17% vs 5%), cough (15% vs 6%), flushing (14% vs 3%), rigors (10% vs 2%), pruritus (10% vs 1%), neutropenia (8% vs 3%), and chest tightness (7% vs 1%).[1]

RITUXAN in Combination with CHOP Chemotherapy for DLBCL

The following adverse reactions, regardless of severity, were reported more frequently (≥5%) in patients age ≥60 years receiving R-CHOP as compared to CHOP alone: pyrexia (56% vs 46%), lung disorder (31% vs 24%), cardiac disorder (29% vs 21%), and chills (13% vs 4%). In the GELA LNH 98-5 study, a review of cardiac toxicity determined that supraventricular arrhythmias or tachycardia accounted for most of the difference in cardiac disorders (4.5% for R-CHOP vs 1.0% for CHOP).[1]

The following Grade 3 or 4 adverse reactions occurred more frequently among patients in the R-CHOP arm compared with those in the CHOP arm: thrombocytopenia (9% vs 7%) and lung disorder (6% vs 3%). Other Grade 3 or 4 adverse reactions reported more frequently among patients receiving R-CHOP were viral infection (GELA LNH 98-5 study, neutropenia (GELA LNH 98-5 and MInT studies), and anemia (MInT study).[1]

Attention Healthcare Provider: Provide Medication Guide to patient prior to RITUXAN infusion.

For additional safety information, please see the full prescribing information, including **BOXED WARNINGS** and Medication Guide, available at this exhibit.

Reference: 1. RITUXAN® (Rituximab) full prescribing information, Genentech, Inc., 2008.

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